

REMARKS

This application has been amended and is believed to place it in condition for allowance at the time of the next Official Action.

Claim Rejections - 35 USC § 112, 1st Paragraph

Claims 33, 34, and 36-54 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention, i.e., this is a NEW MATTER rejection.

The Examiner states that the feature "determining parameters ... , using data stored in said database, said determined parameters including optimized proportions ... for better tolerance ... and greater reaction speed, using the subject's immunity data stored in the database" is new matter.

The applicant respectfully disagrees. One skilled in the art, having read and understood the specification would recognize that the invention included determining parameters that include "optimized proportions" and determining optimized parameters using "immunity data".

AS to "optimized proportions", one of skill would understand that this relates to optimal proportions and optimal

ratio. From the published application please see the following paragraphs:

[0036] The process of the status-characterizing information is arranged for determining respective optimal proportions of different immunocompetent cells in view of their deferred use, and, for example, can provide with a determination of an optimal ratio between lymphocytes T4 and T8 in view of their deferred use.

[0089] Said batch is the processed to room temperature and immunocompetent cells are put in culture and/or submitted to an ex-vivo process. Parameters of a protocol of re-use are determined by requesting identity data from the cell management database and processing said identity data to determine for example optimal ratio between lymphocytes T4 and T8 for re-injection. In view of a deferred-use therapeutic process for a patient, the cell treatment entity is therefore provided with one or several identified batches of cells from said patient and with determined re-use or deferred-use protocol parameters.

[0096] When a re-use process of immunocompetent cells is prescribed for a human or animal subject, a protocol of deferred-use is determined using data stored in the database with, for example, optimal proportions between each type of cells. Selected immunocompetent cells are then extracted from the personal cell library and, if necessary, processed ex-vivo. When these immunocompetent cells are ready for use, a re-use process

according to the determined personal protocol is effected at instant Tu.

[0099] It has to be noted that a management system according to the invention can be entirely automated, from the collection of information characteristic of the physical and/or biological status of a subject, through the preservation and storage of immunocompetent cells, up to the determination of protocols for deferred-use of said immunocompetent cells. The protocol determination process can be advantageously implemented in an expert system processing past experimental and clinical data related to deferred-use cumulated practice. For example, a deferred-use protocol may comprise as a way of non-limitative example, an optimal time schedule indicating the proposed dates for deferred use depending on collected personal parameters and therapeutic indications for re-use, and biological and technical indications required for cell processing before re-use.

As to determining optimized parameters using "immunity data", see the following:

Abstract A method for ..., said personal library cumulating a sum of immunity information stored in the collected immunocompetent cells, This method further comprises: gathering information characteristic of the status of said human or animal subject, effected before or during the immunocompetent cells collection, and processing said characteristic information for determining parameters of a deferred-use protocol for

immunocompetent cells from said human or animal subject's personal library.

[0007] ... These immunocompetent cells constitute in fact a library, in particular a lymphocyte library, which is enhanced during life, when the body meets foreign organisms, during viral, parasitic or bacterial infections. By means of this "immunity library", the body can minimize the impact of the infections during life. The action mechanism of the immune system is already known. Information are stored in the walls of lymphocytes, as illustrated by the transfer factor and reported by numerous publications. This mechanism also contributes to the defense against malignant cells.

[0021] constituting and enhancing from collected batches a personal library of immunocompetent cells, said personal library cumulating a sum of immunity information stored in the walls of the collected immunocompetent cells,

[0029] By means of the successively collected batches of immunocompetent cells from a person, a personal library is therefore constituted for said person. This personal library, which gathers immunity information stored in the walls of the collected immunocompetent cells, can be accessed on demand, when required for a therapeutic protocol, in order to provide with pertinent immunity concerning the patient.

[0031] The status-characterizing information is processed to determine a subject's identity data, for example by

extracting from said status-characterizing information relevant data on personal immunity history and data. The subject's identity data may include immunity-related data, historical and clinical data on previous diseases, treatments and therapeutic protocols experienced by said subject.

[0035] The status-characterizing information and the immunity information stored in the immunocompetent cells of said human or animal subjects are advantageously entered into an expert system used for determining parameters for deferred-use protocols. This expert system can be arranged for providing an interpretation of said status-characterizing information and said immunity information with respect to a particular gene.

The above are examples to show that, when read as a whole, one of skill would see that the feature "determining parameters ... , using data stored in said database, said determined parameters including optimized proportions ... for better tolerance ... and greater reaction speed, using the subject's immunity data stored in the database" is not new matter.

As to claim 33 and how the "deferred use" feature is recited, the claim is a system and recites a status-characterizing information device **processing** said status-characterizing information to determine said subject's identity data, ..., said status-characterizing information device comprising an expert system wherein said status-characterizing information

corresponding to said subject are entered in the form of biological items to which a set of rules stored in a knowledge base is applied, implementing into said expert system a process for determining a deferred-use protocol, said deferred-use protocol comprising biological and technical indications required for cell processing before re-use of a batch of immunocompetent cells previously collected from said subject. The functional aspect of this claim is not indefinite.

The same is true as to "determining parameters" in claims 33 and 36.

Withdrawal of this rejection is therefore solicited.

Claim Rejections - 35 USC § 112, 2nd Paragraph

Claims 33, 34, and 36-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims that depend directly or indirectly from claims 33 and 36 are also rejected due to said dependence.

The Examiner states that the feature "deferred use protocols" is not defined in the specification and interprets this feature as "medical treatment recommendation".

The applicant respectfully disagrees. Indeed, it is clear in the specification that the "deferred-use protocols" concerns a future use of cells in a person and indicates how and

in which conditions (concerning the cells and the person) to introduce the cells in the body of a person whereas a medical treatment recommendation is directed to a person and indicates how to use this medicine.

There is a huge difference between these two features. Indeed, in a medical treatment recommendation, the medicine is known and is constant and the only variable parameter taken into account is the state of the person, generally at the moment the recommendation is given.

In the case of the deferred use protocol of cells, the state of the person at the moment of the re-use is not the only parameter. The deferred use protocol also concerns the re-used cells, the state of the person at the moment the cells have been taken, potential treatment of the cells before injection, etc. All these parameters are variable and differentiate the feature "deferred-use protocol" from the feature "medical treatment recommendation".

See paragraph [0032]: The deferred-use protocol comprises, as a way of non limitative example, a plurality of steps or sequences for retrieving and reconditioning previously stored and preserved batches of immunocompetent cells in view of using said cells for re-injection, and steps for processing the subject's identity data in order to determine for example what type of immunocompetent cells must or can be used with regards to the object of said deferred-use for a given patient, and how and

when such selected immunocompetent cells have to be injected in relation with the patient's health status. This protocol can implement deferred-use parameters such as qualitative and quantitative data on the reconditioned immunocompetent cells, and physiological parameters related to the subject's health status in view of cell auto-use. Also see at least application paragraph [0089], [0096].

At least for these reasons, the broad interpretation of the feature "deferred-use protocol" by the Examiner is erroneous.

The remaining claims were amended consistent with the kind suggestions provided by the Examiner.

Withdrawal of this rejection is therefore solicited.

Claim Rejections - 35 USC § 103

I. Claims 33, 36, 37, 38, 39, and 43 stand rejected under 35 U.S.C. 103(a) over Lefesvre et al. (WO/1999/053030), in view of Winkel (Clinical Chemistry, 1989, 35/8, p.1595-1600), and in view of Adrion et al. (US 5,023,785).

II. Claims 34 and 40 stand rejected under 35 U.S.C. 103(a) over Lefesvre et al. (WO/1999/053030), in view of Winkel (Clinical Chemistry, 1989, 35/8, p.1595-1600), and in view of Adrion et al. (US 5,023,785), as applied to claims 33, 36, 37, 38, 39, and 43, , and further in view of Zanin et al. (WO/1997/045056), and in view of Cha et al. (Physiol. Meas., 1994, Vol. 15, p. 129-137).

III. Claim 42 stands rejected under 35 U.S.C. 103(a) over Lefesvre et al. (WO/1999/053030), in view of Winkel (Clinical Chemistry, 1989, 35/8, p.1595-1600), in view of Adrion et al. (US 5,023,785), in view of Zanin et al. (WO/1997/045056), and in view of Cha et al. (Physiol. Meas., 1994, Vol. 15, p. 129-137), as applied to claims 33, 34, 36, 37, 38, 39, 40, and 43, , and further in view of Tomoyasu (Applied And Environmental Microbiology, Jan. 1998, p. 376-382).

IV. Claims 41 and 44-54 stand rejected under 35 U.S.C. 103(a) over Lefesvre et al. (WO/1999/053030), in view of Winkel (Clinical Chemistry, 1989, 35/8, p.1595-1600), in view of Adrion et al. (US 5,023,785), in view of Zanin et al. (WO/1997/045056), and in view of Cha et al. (Physiol. Meas., 1994, Vol. 15, p. 129-137), in view of Tomoyasu (Applied And Environmental Microbiology, Jan. 1998, p. 376-382), as applied to claims 33, 34, 36, 37, 38, 39, 40- 43, , and further in view of Privitera et al. (US 4,826,760) and Barocci et al. (Transpl. Int., 1993, 6:29-33).

Traverse

Applicant attaches a Declaration of Professeur Dominique CHARRON. Should the format of this declaration not be acceptable, applicant will provide another copy in standard Rule 132 format. However, applicant intends for this declaration to be a Rule 132 declaration.

In summary, the Examiner rejects all the claims as being unpatentable under 35 USC 103(a) over:

Lefesvre (WO 99/53030) in view of
Winkel (Clinical Chemistry, 1989, 35/8, p.1595-1600) in view of
Adrion et al. (US 5,023,785), or further in view of
Zanin et al. (WO 97/45056), still in view of
Cha et al. (Physiol. Meas., 1994, Vol.15, p.129-137),
Tomoyasu (Applied and Environmental Microbiology, Jan. 1998,
p. 376-382),
Privitera et al. (US 4,826,760), and
Barocci et al. (Transpl. Int., 1993, 6:29-33).

The rejection indicates that Lefesvre is considered as being the closest prior art.

The rejection recognizes that Lefesvre doesn't teach:

i) an expert system that uses biological items and applies a set of rules stored in a knowledge base;

ii) an expert system that determines a deferred-use protocol comprising biological and technical indications required for cell processing; and

iii) a processor determining parameters of deferred-use protocol including optimal proportions of various selected cell types using the subject's immunity data.

Applicant will discuss the secondary references and their shortcomings.

Winkel

The rejection states that Winkel discloses an expert system applied to clinical data and produces treatment recommendations.

From there, the rejection states that Winkel discloses the feature **ii)**, i.e. "an expert system that determines a deferred-use protocol comprising biological and technical indications required for cell processing"

Applicant respectfully disagrees.

Winkel teaches several expert systems applied to clinical data. Some of the expert systems disclosed in Winkel provide diagnostic results and treatment recommendations. At page 1597 col. 2, Winkel discloses a Table listing the most known expert systems emphasizing the use of laboratory data.

However, none of the expert systems listed in this table is used in the domain of the reuse of cells, or the processing of parameters of a cell re-use protocol.

The Examiner's attention is directed to MPEP § 2111 for guidance in giving the pending claims their broadest reasonable interpretation consistent with the specification, e.g., "deferred use protocols". In analyzing the claims, the rejection fails to properly interpret the claims' terms. More specifically, the rejection gives the meaning of the terms in the claims a meaning inconsistent with in the specification.

The MPEP § 2111 guidance does not authorize that the claim terms can take on any conceivable meaning the Examiner may create. The Examiner is limited such that the broadest reasonable interpretation of the claims is consistent with the interpretation that those skilled in the art would reach. *In re Cortright*, 165 F.3d 1353, 1359, 49 USPQ2d 1464, 1468 (Fed. Cir. 1999).

Taking into account the meaning of the feature "deferred use protocols" reminded in paragraph 2, Winkel doesn't teach "deferred use protocols" for cells. So Winkel doesn't teach "an expert system that determines a deferred-use protocol comprising biological and technical indications required for cell processing".

Thus, the feature ii) is not disclosed in Winkel.

Moreover, Winkel repeatedly states that the adaptation of an expert system designed for a given domain for use in a different domain is very difficult and can only be done if the requirements imposed by the problem are understood (see p. 1597 col. 2 §3, p. 1598 col. 1 §2 §3 "the appropriate tool can be chosen only after requirements imposed by the problem are understood"). Finally, Winkel states as a conclusion that "the development of transparent systems ... that may be transferred between technical and medical environments and easily updated and modified by the end user **represents a real challenge**" (p.1599, col. 2, §2).

This is an objective evidence that the adaptation of the expert systems of Winkel for use in the domain of the re-use of cells in not obvious.

Adrion

Adrion teaches an expert systems outputting diagnostic information of a patient. In claim 4, Adrion discloses the name of the parameters taken into account in the diagnostic.

The rejection states that Adrion teaches optimized parameters comprising the cell ratio amounts based on claim 1 and claim 5.

The Applicant respectfully disagrees.

Adrion teaches an expert system outputting diagnostic information of a patient in the domain of hematology.

However, the apparatus disclosed in Adrion comprises data processing means for "evaluating blood derived parametric values" and "means for "ascertaining clinically interval combination". Adrion doesn't determine optimal proportions of cell types, but only combination of intervals.

In claim 4 of Adrion, the expression "lymphocyte/monocyte count" doesn't mean the ratio of lymphocyte/monocyte.

Indeed the expression "lymphocyte/monocyte count" means "lymphocyte or monocyte count". This interpretation is confirmed in claim 5 of Adrion where it is stated that the "...lymphocyte/monocyte count... is expressed in $\times 10^9/L$ ". Indeed, if

it was the ratio the count wouldn't be expressed in "/L" and wouldn't have any measurement unit.

At least for these reasons, Adrion doesn't disclose "determining parameters of deferred-use protocol including optimal proportions of various selected cell types using the subject's immunity data".

Thus, Adrion doesn't disclose feature iii).

Conclusions

From the above, it is shown that Winkel doesn't teach feature ii), and Adrion doesn't teach feature iii).

Moreover, the above further shows that there is objective evidence in Winkel that the combination of different expert systems designed for different domains is not obvious for a person having ordinary skills in the art and represents a real challenge.

Accordingly, Applicant respectfully submits that neither independent claim 33 nor claim 36 is rendered obvious over Lefesvre et al., in view of Winkel and Adrion.

The attached Declaration of Professeur Dominique CHARRON is offered as further evidence of the claims being non-obvious.

Reconsideration and allowance of all claims are respectfully requested.

Summary

In view of the foregoing Remarks, applicant believes that the present application is in condition for allowance. Allowance and passage to issue is respectfully requested.

Applicant invites the Examiner to contact the undersigned Attorney by telephone to discuss the case, should the Examiner believe that the case can be advanced by such a discussion.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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APPENDIX:

The Appendix includes the following item:

- a Declaration of Professeur Dominique CHARRON